IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of
Mamoru OHASHI et al
Serial No.: 09/529,715
Filed: April 19, 2000
For: FAST-DISSOLVING PHARMACEUTICAL COMPOSITION

Group Art Unit: 1616
Examiner: S. Gollamudi

DECLARATION

Honorable Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

I, Mamoru OHASHI, a citizen of Japan residing at 24-20-303, Shioe 2-chome, Amagasaki-shi, Hyogo-ken, Japan, declare as follows.

1. I was graduated from Kyoto Pharmaceutical University in March 1988, and completed the master's course at the same university in March 1990.

Since April 1990 up till the present, I have been an employee of Dainippon Pharmaceutical Co., Ltd. and had been engaged in researches and developments of drug product formulation, particularly in solid dosage form. I am now an assistant chief of Formulation Group in Pharmaceutical Research Laboratory of said company.

2. I am one of the coinventors for the invention described in U.S. Serial No. 09/529,715 and am familiar with the subject matter thereof.

3. I have read the cited Negoro et al., U.S. Patent 5,258,382, Muller at el., U.S. Patent 5,858,410 and Schneider et al., U.S. Patent 5,356,636 and

am familiar with the subject matter thereof.

4. Under my direction, the following comparative experiment has been done.

Experiment

1. Preparation of test compositions (tablets):

(1) Preparation of tablets of the present invention (Tablet A)

AS-3201 crystals prepared in a similar manner as disclosed in Example 1 of U.S. Patent 5,258,382 were micronized using Single Truck Jet Mill (manufactured by SEISHIN ENTERPRISE CO., LTD.) with compression air pressure of 6 kgf/cm^2 to give powders having a mean particle size of about 1.5 μm. By using the micronized AS-3201, tablets were prepared by the following formulation.

Components	Amount
Micronized AS-3201	160 g
Tartaric acid	8 g
Lactose	492 g
Low substituted hydroxypropylcellulose	300 g
Hydroxypropylcellulose	20 g
Magnesium stearate	20 g
Total	1000 g

The micronized AS-3201 powders, lactose and low substituted hydroxypropylcellulose were charged into a fluid bed granulator and drier, and then the mixture was granulated by spraying thereto a solution of tartaric acid in a 5% aqueous hydroxypropylcellulose solution. The granules were dried and thereto was added magnesium stearate, and the mixture was blended in a V-blender. The resultant was compressed on a rotary tableting machine to give tablets weighting 125 mg and containing 20 mg of AS-3201 in each tablet.

(2) Preparation of tablets of the present invention (Tablet B)

AS-3201 crystals prepared in a similar manner as disclosed in Example 1 of U.S. Patent 5,258,382 were micronized by Sample Mill (manufactured by HOSOKAWA MICRON CORPORATION) to give powders having a mean particle size of about 10 μm. By using the micronized AS-3201, tablets were prepared in the same manner as described in the above preparation of Tablet A.

(3) Preparation of tablets of the reference composition (Tablet C)

By using AS-3201 crystals prepared in a similar manner as disclosed in Example 1 of U.S. Patent 5,258,382 (which had a mean particle size of about 87 μm), tablets were prepared in the same manner as described in the above preparation of Tablet A.

2. Dissolution Test:

The dissolution of the active AS-3201 from the tablets obtained above was evaluated according to Padddle method (50 rpm) specified in the Twelfth Edition of the Pharmacopoeia of Japan, using a 0.2 M phosphate buffer (pH 6.5, 900 ml) as a test solution. The quantitative assay of AS-3201 was carried out by spectrophotometry at 300 nm.

3. Test results:

The results are shown in the attached Fig. 1. Each point of Fig. 1 shows the mean value of the results in three repeats of the experiments on each of Table A, Table B and Tablet C.

As is shown in Fig. 1, the tablets (Tablet A, Tablet B) of the present invention showed remarkably improved dissolution characteristics in comparison with the Tablet C of the reference composition.

The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

This 12 day of March, 2003.

Mamoru Ohashi

Mamoru Ohashi